IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF	:	Colin Gerald Caro et al.
FOR	:	**STENTS FOR BLOOD VESSELS**
SERIAL NO.	:	09/857,012
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EXAMINER	:	Paul B. Prebilic
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DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The undersigned declares as follows:

1. My name is Colin Gerald Caro. I am Professor Emeritus of Physiological Mechanics and Senior Research Investigator at Imperial College London, United Kingdom.

2. I have been the author of many scientific publications during my 40 year career at Imperial College.

3. Prior to my time as a Professor at the Imperial College of Science, Technology and Medicine, I was a hospital doctor at teaching hospitals, including St Thomas's Hospital, London

4. Overall, I have published approximately 200 papers dealing with circulatory physiology. I am also listed as an inventor on about 20 patents. I am also one of the inventors of the instant application.

5. Among other professional activities, I am an Initial Foreign Fellow of the American Institute of Medical & Biological Engineering; a Founding Fellow of the International Academy of Medical & Biological Engineering; an Honorary Fellow of the Institute of Physics and Engineering in Medicine; an Honorary Fellow of the

International Society of Cardiovascular Medicine and Science (recipient of the Arthur Guyton Award). I have been awarded Honorary Doctorates from the University of London and the University of Paris. I have been International Chairman of the World Council of Biomechanics and Vice President of the International Society of Biorheology, Recently, I have been Chairman of the Imperial College Imaging Sciences Centre and Chairman of the Imperial College Cardiovascular Technology Network.

6. In one aspect, the instant application, as recited in claim 47, pertains to a stent for insertion into a blocked, constricted or otherwise flow restricted vessel. It comprises:

a. a hollow tube which is capable of supporting an interior wall of the vessel;

b. a plurality of openings located in the wall of the tube so that the interior wall of the vessel is exposed via said openings to a fluid flow along the vessel; and,

c. wherein the hollow tube is preshaped so as to have an at least partially helical shape, and wherein a central axis of the hollow tube forms a non-planar three-dimensional at least partially helical shape and the hollow tube is capable of imposing said three-dimensional at least partially helical shape on a central axis of the vessel so that a swirling fluid flow is introduced within the vessel.

7. An earlier document about which I am knowledgeable is International Publication No. WO 95/09585 (International Application Number PCT/GB94/02023, the PCT application). I am the inventor of the vascular prostheses described in that PCT application. As is evident from Figure 6, in one embodiment, a prosthesis includes a tube 1 with a non-planar curved portion 5, which is employed to bypass an internal blockage 7 in an artery 6.

8. I note in the PCT application that in order to maintain the tubing 1 open and prevent collapse or kinking, it is possible to use a stent or other structural support of plastic, metal or other material internally, externally or integral to the wall of the tubing.

9. At the time of filing of the PCT application the only stents of which I was aware were cylindrical stents. If that cylindrical stent was at all rigid, it would impose its shape on the non-planar curved shape of the tube 1, reducing the curvature of the tube. As

might be expected, this is disadvantageous, since it would harm the circulation by lessening the swirling flow of the fluid passing through the prosthesis formed by the hollow tubing 1. If, on the other hand, the stent was very flexible, it would simply adopt the non-planar curvature of the tubing 1.

10. I believe it would be difficult to remove a stent once it is inserted within the tubing. But, if someone could remove such a stent from inside the tubing 1, the stent, whether it was rigid or flexible, would again assume its normal cylindrical shape. In other words, the stent would not maintain any change imposed on the stent's normal cylindrical shape by the tubing, once the stent was removed from the tubing.

11. Another patent showing a cylindrical stent is U.S. Patent No. 5,354,308 of Simon et al. The Simon et al. patent pertains to a conventional metal wire stent which is cylindrical or tubular in configuration as shown in the several drawings in Simon et al. Figure 6 of Simon et al. shows a sleeved stent in which a compressive sleeve 22 is positioned around a skeletal frame 2 of a stent. The entire structure is, however, cylindrical in shape.

12. A still further patent which discloses a cylindrical stent is the Fontaine 5,443,498 patent. The Fontaine patent also mentions a curved stent in column 6, lines 14-19. The stent disclosed would appear to have a central axis which possesses a 2 dimensional or planar curvature. However, such planar curvature would not induce a swirling flow, as a three dimensional curvature is required to do so.

13. In contrast to the conventional cylindrical stents shown in Simon et al. and Fontaine, and contemplated by me in the PCT application, the stent according to the instant application is a hollow tube that is pre-shaped (including being formed from a shape-memory alloy) so as to have an at least partially helical shape so that a central axis of the hollow tube forms a non-planar three-dimensional at least partially helical shape. This is illustrated in the side-by-side photographs of a conventional stent and a helical stent according to the instant application, enclosed as Exhibit A hereto.

14. The PCT application also mentions that a hollow body portion 9 has a non-planar curved branch member 8. The hollow body portion 9 may be inserted within a vein or artery either for receiving flow of blood from the branch member 8 or for delivering a flow of blood to the branch member, wherein a swirl flow is established within the non-planar curved branch member. It should be noted that while the hollow

body portion 9 may be inserted within a vein or artery, the curved branch member 8 is not. Rather, the free end of it is sutured to an adjacent blood flow conduit. In any case, any stent would be located within the curved branch member, which substitutes as a blood flow conduit for the patient.

15. There are many differences between the prosthetic tube 1 illustrated in my PCT application and the stent of the instant application. The prosthesis is used to bypass or replace a blocked portion of an artery or vein, as shown in Figure 6. In contrast, the stent of the current application is used to impose a three-dimensional, at least partially helical shape on a central axis of a blocked, constricted or otherwise flow restricted vessel. In other words, while a prosthesis bypasses the patient's vessel, the stent opens up the patient's vessel and gives the desired flow characteristics to the fluid flowing in the vessel. Such flow characteristics, namely, the swirling fluid flow induced within the vessel, is useful to prevent restenosis. Restenosis is the reoccurrence of stenosis, an abnormal narrowing of a blood vessel or other tubular organ or structure.

16. In fact, the prosthesis of my PCT application and the stent of the instant application are used to treat completely different diseases. I should note that these diseases are treated by different medical specialists. The prosthesis is used to treat intimal hyperplasia whether for example at an arterial bypass graft or, as shown by our recent work, at vascular access grafts in patients with end-stage renal disease undergoing hemodialysis. Enclosed as Exhibit B hereto, please find a recent article of which I am a co-author entitled "Preliminary Comparative Study of Small Amplitude, Helical and Conventional ePTFE Arteriovenous Shunts in Pigs." This article was published on-line by Interface, a Journal of The Royal Society of London on 16 May 2005. Photographs in the article show model grafts and a graft made according to my PCT application.

17. However, at the time my PCT application was filed, neither I nor anyone else had any thought of forming stents into a non-planar, three-dimensional at least partially helical shape, so as to be capable of imposing the three-dimensional at least partially helical shape on the central axis of a vessel, in order to introduce swirling fluid flow within the vessel and expose its interior wall to the swirling fluid flow.

18. Enclosed as Exhibit C hereto are photographs illustrating both straight stent and helical stents according to the present application one month after implant in

two animal subjects. The stents were made by the same manufacturer and were initially identical in design, but one was unchanged after laser cutting and the other was formed into a helical shape. A straight stent was implanted in one carotid artery and a helical stent was implanted in the opposite carotid artery in the same animal to permit comparison of the histopathology of the two stented vessels. The average thickness of the intima in the carotid artery segments which were stented was 0.2731mm for the straight stent and 0.1484mm for the helical stent. In another animal, helical stents were implanted in both carotid arteries. The average intimal thickness was 0.0777mm in the left carotid artery and 0.0577mm in the right carotid artery. In these preliminary studies there was a trend towards less pathological wall thickening in the helical stent than in the straight stent. In the first animal the percentage stenosis in the straight stent was 36% and in the helical stent the percentage stenosis was 20%. In the second animal the percentage stenosis for the two helical stents was 15% and 14% for the left and right carotid arteries respectively. These intimal thickness and stenosis values were obtained by taking the average of measurements from sections taken at the proximal, middle and distal ends of the stented vessel segments as shown in Exhibit C.

19. The stent, when installed in a test subject, imposes a three-dimensional at least partially helical shape on a central axis of a vessel so that a swirling fluid flow is induced within the vessel. The benefits conferred by the stent according to the instant application should be apparent. There is not the need to employ a graft or prosthesis to achieve the desired flow characteristics in the patient. Instead, an advantageously designed stent can be used, saving the patient's own vessel. With the stent according to the present application, restenosis is hindered by the swirling fluid flow induced within the stented vessel, unlike with conventional cylindrical stents.

20. In my view, a stent according to the instant application confers benefits much different from those conferred by my PCT application. More particularly, the prostheses disclosed in my PCT application replace a blocked, constricted or otherwise flow restricted vessel. In contrast, the stent of the instant application opens up a patient's blocked, constricted or otherwise flow restricted vessel. Thus, the patient's own vessel is used in treating the pathology, employing the stent of the instant application, rather than needing to replace or bypass the patient's diseased vessel by the prosthesis of my PCT application.

21. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

By Colin G Caro

Printed Name: Colin G Caro

Date: June 15th 2007

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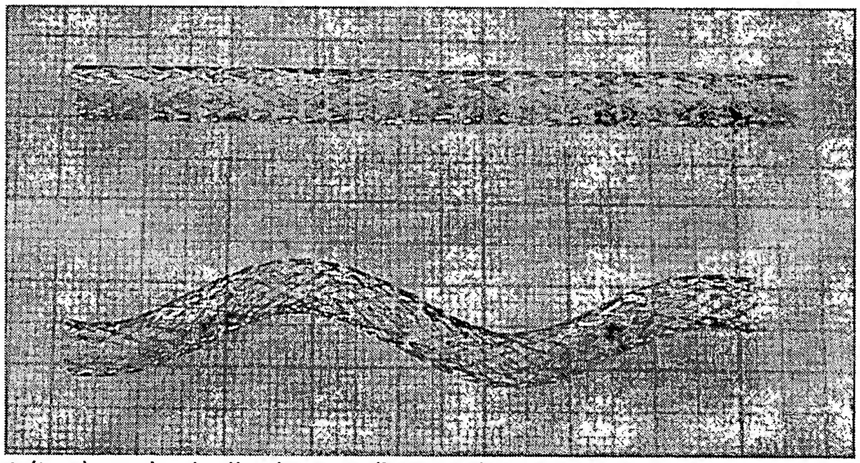
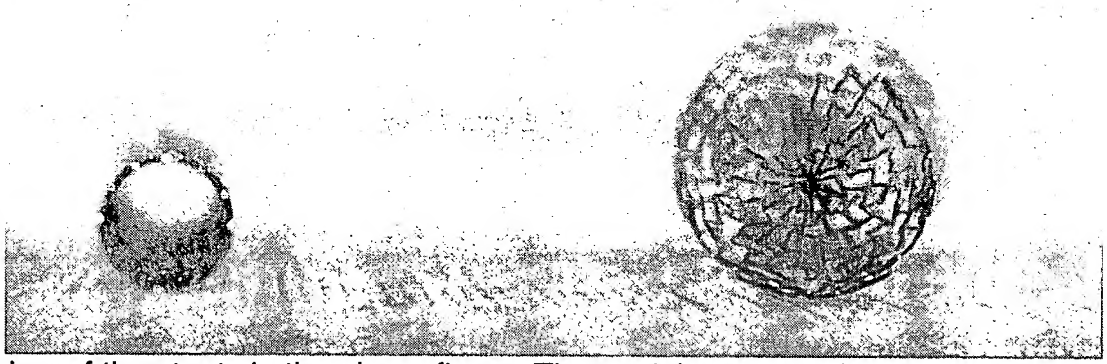
EXHIBIT A



A straight stent (top) and a helical stent (bottom). The patterns in both stents were identical prior to heat setting.



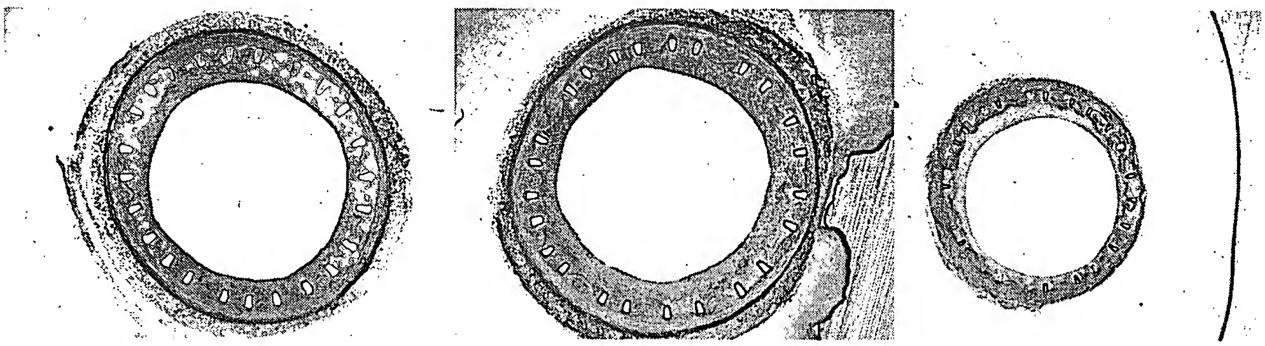
End view of the stents in the above figure. The straight stent is shown on the left and the helical stent is shown on the right.

EXHIBIT B

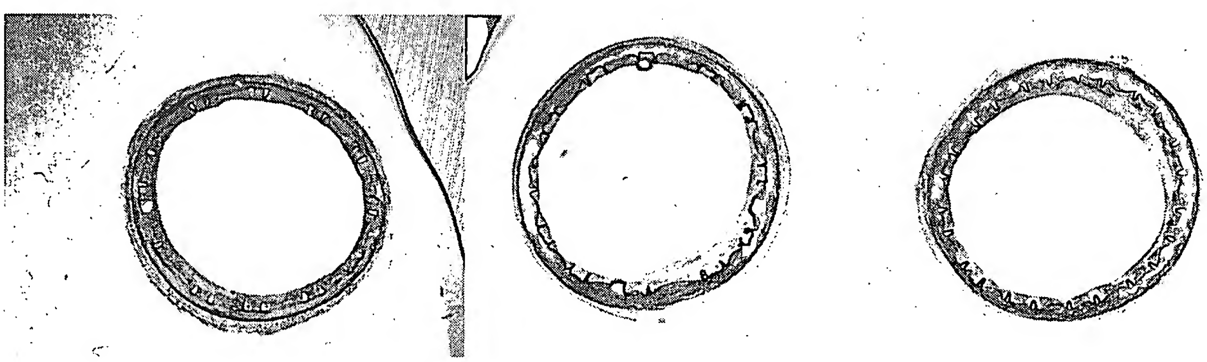
Refer to journal article attached in pdf format.

EXHIBIT C

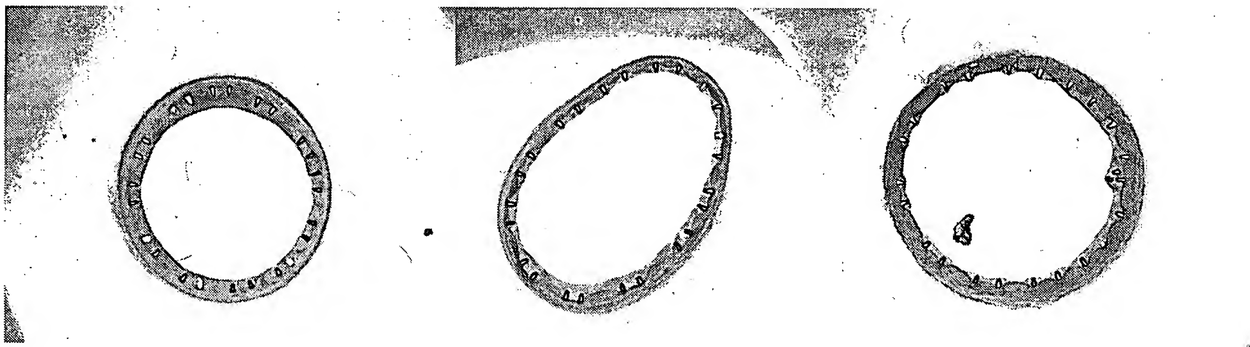
In a small study one straight and three helical stents were implanted in the carotid arteries of two pigs. The following is a summary of the histomorphometry results from the study.



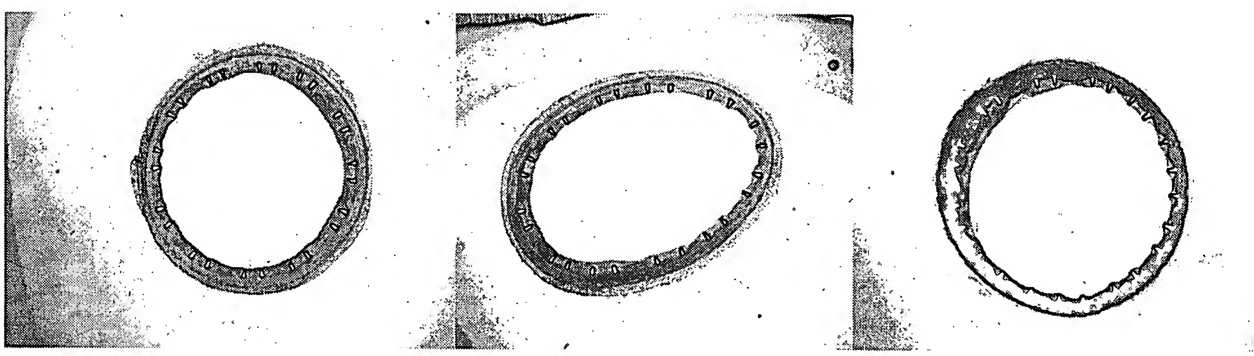
Proximal (left), mid (centre) and distal (right) sections of a straight stent implanted in the left common carotid artery of the first animal and harvested one month after implantation. The mean intimal thickening is 0.2731mm. The mean level of stenosis is 36%. Measurements were averaged over the three sections.



Proximal (left), mid (centre) and distal (right) sections of a helical stent implanted in the right common carotid artery of the first animal and harvested one month after implantation. The mean intimal thickening is 0.1484mm. The mean level of stenosis is 20%. Measurements were averaged over the three sections.



Proximal (left), mid (centre) and distal (right) sections of a helical stent in the left common carotid artery of the second animal, harvested one month after implantation. The mean intimal thickening is 0.0777mm. The mean level of stenosis is 15%. Measurements were averaged over the three sections.



Proximal (left), mid (centre) and distal (right) sections of a helical stent in the right common carotid artery of the second animal, harvested one month after implantation. The mean intimal thickening is 0.0577mm. The mean level of stenosis is 14%. Measurements were averaged over the three sections.